

Docket No.: 2825.2025-001

Title: Association of Thrombospondin..

entors: Stacey Bolk, *et al.*



Nucleotide

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Nucleotide

Protein

Genome

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☐ 1: GI = "4507486" [GenBank] Homo sapiens thrombospondin... PubMed, Protein, Related Sequences, 1

LOCUS NM\_003247 5784 bp mRNA PRI 31-OCT-2000  
DEFINITION Homo sapiens thrombospondin 2 (THBS2), mRNA.  
ACCESSION NM\_003247  
VERSION NM\_003247.1 GI:4507486  
KEYWORDS  
SOURCE human.  
ORGANISM Homo sapiens  
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.  
REFERENCE 1 (bases 1 to 5784)  
AUTHORS LaBell,T.L., Milewicz,D.J., Distech,C.M. and Byers,P.H.  
TITLE Thrombospondin II: partial cDNA sequence, chromosome location, and  
expression of a second member of the thrombospondin gene family in  
humans  
JOURNAL Genomics 12 (3), 421-429 (1992)  
MEDLINE 92217961  
REFERENCE 2 (bases 1 to 5784)  
AUTHORS LaBell,T.L. and Byers,P.H.  
TITLE Sequence and characterization of the complete human thrombospondin  
2 cDNA: potential regulatory role for the 3' untranslated region  
JOURNAL Genomics 17 (1), 225-229 (1993)  
MEDLINE 94010892  
COMMENT PROVISIONAL REFSEQ: This record has not yet been subject to final  
NCBI review. The reference sequence was derived from L12350.1.  
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FIG. 1a

Docket No.: 2825.2025-001

Title: Association of Thrombospondin...

Investors: Stacey Bolk, *et al.*

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/evidence=experimental

/product="thrombospondin 2"

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297..884

/note="TSPN; Region: Thrombospondin N-terminal -like domains"

misc\_feature

297..884

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misc\_feature

1197..1355

/note="vwc; Region: von Willebrand factor type C domain"

misc\_feature

1392..1529

/note="tsp\_1; Region: Thrombospondin type 1 domain"

misc\_feature

1560..1712

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1728..1883

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misc\_feature

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5761..5766

/note="putative"

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polyA\_site

5784

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121 ctgcagggcc ggtctctcgc tccagcagag cctgcgcctt tctgactcgg tccggaacac  
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FIG. 1b

Docket No.: 2825.2025-001

Title: Association of Thrombospondin...

Inventors: Stacey Bolk, *et al.*

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3661 atgaccaaac ctacgtggc gggcggctgg gtctatttgt cttctctcaa gaaatggctc  
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3841 ctctctctag cagcacctcc tgtcccttga ccttaactct gatggttctt cacctcctgc  
3901 cagcaacccc aaacccaagt gccttcagag gataaatatc aatggaactc agagatgaac  
3961 atctaaccce ctagaggaaa ccagtttggg gatatatgag actttatgtg gagtgaatat

FIG. 1c

Docket No.: 2825.2025-001

Title: Association of Thrombospondin...

Authors: Stacey Bolk, *et al.*

4021 tgggcatgcc attacattgc tttttcttgt ttgttttaaaa agaatgacgt ttacatatataa  
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4201 actattcttg aattagagtt gctctacaat gacacacaaa tcccgctaaa taaattataa  
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5641 gaaacgtcat gtgttttgcc aaagactgta aatatttatt tatgtgttca catgggtcaaa  
5701 atttcaccac tgaaaccctg cacttagcta gaacctcatt tttaaagatt aacaacagga  
5761 aataaattgt aaaaaaggtt ttct (SEQ ID NO: 1)

FIG. 1d

## Novel association found in Gene Quest with thrombospondin 2 (THBS2)

**Association**

Odds ratios (with 95% confidence intervals) for association of THBS2 genotypes with CAD and MI in the Gene Quest population.

THBS2	CAD cases	controls	Odds ratios (95% C.I.)	P value	adjusted ORs (95% C.I.)	P value
tt	160 (.48)	207 (.51)	1.0	-	1.0	-
tg	153 (.46)	158 (.39)	1.25 (.93-1.70)	.15	1.24 (.88-1.76)	.23
gg	17 (.05)	39 (.10)	.56 (.31-1.03)	.06	.65 (.34-1.26)	.20

\* $\chi^2$  p value=.025

THBS2	MI cases	controls	Odds ratios (95% C.I.)	P value	adjusted ORs (95% C.I.)	P value
tt	84 (.47)	207 (.51)	1.0	-	1.0	-
tg	87 (.49)	158 (.39)	1.36 (.94-1.95)	.10	1.38 (.92-2.09)	.12
gg	6 (.03)	39 (.10)	.38 (.16-.93)	.03	.39 (.15-1.03)	.06

\* $\chi^2$  p value=.0085

\*the  $\chi^2$  statistic tests for a difference in the distribution of genotypes in the table of data

CAD=coronary artery disease

MI=myocardial infarction

Adjusted ORs=adjusted odds ratio

Heterozygotes show a (non-significant) trend for increased risk of MI. Homozygotes for the variant allele (g) appear to have a significant protective effect. Both of these effects are independent of BMI, hypertension, diabetes, current age and gender (see Oradj).

**Multivariate logistic regression taking all three THBS genes into account for their association with MI.**

GENOTYPE	N	OR (MI)	P (MI)
TSP1_NN	177	1.00	-
TSP1_SN	52	1.07	.76
TSP1_SS	5	8.44	.06
TSP2_tt	103	1.00	-
TSP2_tg	106	1.54	.03
TSP2_gg	9	0.51	.12
TSP4_AA	133	1.00	-
TSP4_AP	94	1.79	0.004
TSP4_PP	14	1.54	.31

FIG. 2